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Risk and prognostic factors for non-specific musculoskeletal pain: A synthesis of evidence from systematic reviews classified into ICF dimensions

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ABSTRACT

A wide variety of risk factors for the occurrence and prognostic factors for persistence of non-specific musculoskeletal pain (MSP) are mentioned in the literature. A systematic review of all these factors is not available. Thus a systematic review was conducted to evaluate MSP risk factors and prognostic factors, classified according to the dimensions of the International Classification of Functioning, Disability and Health. Candidate systematic reviews were identified in electronic medical journal databases, including the articles published between January 2000 and January 2008 that employed longitudinal cohort designs. The GRADE Working Group's criteria for assessing the overall level of evidence were used to evaluate the reviews. Nine systematic reviews were included, addressing a total of 67 factors. High evidence supported increased mobility of the lumbar spine and poor job satisfaction as risk factors for low back pain. There was also high evidence for intense pain during the onset of shoulder and neck pain and being middle aged as risk factors for shoulder pain. High evidence was also found for several factors that were not prognostic factors. For whiplash-associated disorders these factors were older age, being female, having angular deformity of the neck, and having an acute psychological response. Similarly, for persistence of low back pain, high evidence was found for having fear-avoidance beliefs and meagre social support at work. For low back pain, high evidence was found for meagre social support and poor job content at work as not being risk factors.

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1. Introduction

Work is viewed as being beneficial for health and for social economic status [168]. However, when musculoskeletal pain (MSP) is present, work can be burdensome, resulting in reduced productivity, increased sick leave, and high costs for society [28,56,121]. Obtaining better knowledge of risk factors for the onset of MSP and prognostic factors for the persistence of MSP could provide tailored interventions [59,94,138].

In a healthy population various risk factors of MSP exist. As soon as MSP emerges, it may run its normal course; but in some people, pain lasts longer and may become chronic. These influencing factors are called prognostic factors. Several theoretical models have been proposed that describe the development and prolongation of MSP [72,122,162]. Some reflect contradictory theoretical relationships between the cause and the consequence of MSP. For example,

Waddell's biopsychosocial model is based on neurophysiological or physiological dysfunction [162]. A work-related model is Kasarek's Job Control-Demand model [72]. This situation-centred psychosocial model assumes that a disbalance between high job demands and low worker control results in poor subjective health. A person-centred model is the catastrophizing hypothesis model, which posits that fear of pain results in self-limitation of activity and could therefore be a prognostic factor [122]. All these models have their own paradigm, which may possibly lead to confusion. The International Classification of Functioning, Disability and Health (ICF), however, lacks a paradigm [168]. Instead of explaining causal relationships, the ICF classifies them (Fig. 1) [168]. Therefore the ICF can be used to disentangle a diversity of relationships.

The variety and the number of factors stated in the different ICF dimensions make it difficult for healthcare professionals to judge the relative importance of different risk and prognostic factors [27]. Moreover, several medical disciplines have their own guideline recommendations for employers and patients. These guidelines focus on different risk and prognostic factors [12,84,161]. For example, occupational guidelines for preventing low back pain (LBP) list physically or psychologically demanding work as causal

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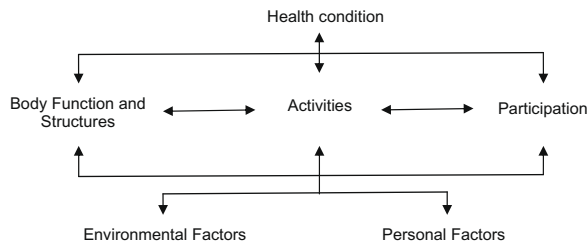


Fig. 1. International Classification of Functioning, Disability and Health [168].

factors of MSP [161]. By contrast, the Dutch physical therapist guideline for LBP lists pain behaviour, fear avoidance and patients' social environment as prognostic factors [12], whereas the clinical guideline of the Norwegian Back Pain Network lists heritage, life-style and low physical activity as risk factors for acute LBP [84]. The guidelines are based on several levels of evidence, from authority-based judgements to systematic reviews of longitudinal and transversal studies. Currently a thorough overview of these predictive factors, regardless of specialism, is lacking. This could result in clinicians being ill informed of how to correctly advice patients and employers to appropriately consider risk and prognostic factors during treatment.

The aim of this review was to qualify and classify the evidence presented in systematic reviews of risk and prognostic factors for non-specific MSP within the ICF. We summarised the evidence, providing a meta-perspective of existing evidence for factors. Missing components in the model may motivate further research into that specific classification domain.

2. Methods

2.1. Search strategy

A systematic review (SR) is considered to be the highest level of evidence [108]. Many overviews of risk and prognostic factors have been published. For this reason, only SRs were included in this review. To identify relevant SRs, we performed an electronic search of bibliographic literature databases (MEDLINE, CINAHL, EMBASE, and PsycINFO), using keywords, MeSH and free text words (Supplementary Appendix 1) from January 2000 up to January 2008. A sensitive search filter for SRs was used [59]. Additional references of guidelines of MSP and all identified SRs were screened for potential eligible studies.

2.2. Selection of studies

Only full reports written in English and meeting the following inclusion criteria (based on study design, population, and exposure) were selected.

2.2.1. Design

Longitudinal research is the preferred method for identifying causal relationships [94]. Therefore, SRs that summarised prospective or retrospective cohort studies were included in our present review. A SR was defined as a review of studies that systematically searched for evidence, that was based on methodological quality assessment of the included studies and that summarised the findings according to predetermined criteria. We considered a meta-analysis to be a type of SR that uses quantitative methods.

2.2.2. Population

Studies that examined adults, aged 18–70 years, with non-specific MSP (as an outcome variable or inclusion criterion) were in-

cluded. Non-specific MSP was defined as MSP not attributed to recognisable, known specific pathology (e.g., infection, tumour, osteoporosis, ankylosing spondylitis, fracture, inflammatory process, radicular syndrome, cauda equina syndrome, and pregnancy) [28,56]. For SRs analysing risk factors, we included those that examined working populations or community-based populations and that identified at least one risk factor and non-specific MSP as an outcome variable. For SRs analysing prognostic factors, we included studies that identified at least one prognostic factor for prolonged MSP. SRs that included workers on 100% sick leave at baseline assessment were excluded. Additional exclusion criteria, such as acute and chronic or severe and non-severe pain at baseline, were not formulated.

2.2.3. Exposure

We included SRs that investigated whether a person's exposure to various factors (body function and structures, activities, participation, personal and environmental factors) predicted MSP. SRs were excluded that examined the impact of treatments. If an SR summarised several factors, we only extracted the findings for factors based on longitudinal cohort studies.

2.3. Study outline

In the first stage, one reviewer (AEL) screened the title and abstract of candidate articles. In the second stage, two reviewers (AEL and RS) screened the full text of all potential relevant articles to determine whether the article met the inclusion criteria. Because the reviewers were familiar with some of the articles, no blinding of authors and institutes was performed.

2.4. Methodological quality assessment of the included systematic reviews

Two reviewers (AEL and TT) independently assessed the quality of the included SRs using the list of criteria for assessing quality, description of potential bias, internal validity, and statistical criteria (Supplementary Appendix 1) [6–8,68]. For each candidate SR, each criterion was rated as 'met' (+), 'unclear/partly met' (±), or 'not met' (–). The total score was calculated by summing up the numbers of 'met'. The total maximum score was 9 points. The methodological quality of an SR was labelled as 'minor limitation' if the quality score was at least 7 out of 9 points and as 'moderate limitations' if the quality score was at least 4 out of 9 points. SRs meeting less than four of the criteria were SRs with 'major limitations' [68]. The inter-rater agreement between the two reviewers was calculated with Cohen's kappa [33]. Agreement was resolved by consensus between AEL and TT. If disagreement persisted after the consensus meeting a third reviewer (MFR) made the final decision.

2.5. Extraction of data

The following data were used for analysis: population characteristics at baseline, date of ending search strategy, number of cohorts and included subjects, study design, methodological quality assessment of included cohort studies, consistency of the available evidence of factors, range of time over which follow-up measurements were made, and outcome measurements. The cohort studies of the included SRs were checked for double counting of extracted risk or prognostic factors based on repetition of cohort studies. When we encountered more than one SR that assessed the methodological quality of the same cohort study, we extracted the cohort study assessments from the SR that was of the highest methodological quality. Identified risk and prognostic factors were classified according to ICF [168]. One reviewer (AEL) extracted the

Table 2
GRADE level of evidence [7,68].

Level of Evidence Quality	Based on:
High-quality evidence	One or more updated, high-quality systematic reviews based on at least 2 high-quality cohort studies ^a with consistent ^b results
Moderate-quality evidence	One or more updated systematic reviews of high or moderate quality based on at least 1 high-quality cohort study based on at least 2 cohort studies of moderate quality with consistent results
Low-quality evidence	One or more systematic reviews of variable quality based on cohort studies of moderate quality based on inconsistent results in the reviews based on inconsistent results in cohort studies
No evidence	No systematic review identified

^a The assessment of the methodological quality of cohort studies was extracted from the included systematic review.

^b Consistent means more than 75% of the included cohorts pointed towards the same direction.

data. To verify accuracy, a second reviewer (RS) selected a random sample ($n = 3$) from the included SRs.

2.6. Level of evidence for each risk and prognostic factor across systematic reviews

The level of evidence and strength of recommendations were assessed according to the criteria assessed by the GRADE Working Group [6,68]. GRADE stands for Grading of Recommendations Assessment, Development and Evaluation. GRADE classifies the level of evidence (high, moderate, low, and none) based on (1) the methodological quality of the SR, (2) the quality of the cohort studies included in the SR, and (3) the consistency of the results of the cohort studies (Table 2). The GRADE level of evidence indicates the extent to which one can be confident that a specific factor predicts MSP or the consequences of MSP.

3. Results

3.1. Literature search

The results of the search strategy are presented in Fig. 2. The literature search of databases resulted in 7937 potentially relevant articles. Excluded on title, abstract and duplicate were 7881 articles. Another 48 articles were excluded after the full text was read. The main reason for exclusion was firstly allowing cross-sectional study design in the reviewed factor of the SR, and secondly non-attendance of methodological quality rating. Screening the refer-

ences of MSP guidelines, all selected articles, and all retrieved SRs resulted in one additional eligible SR. A total of nine SRs were included in the present review [35,53,55,65,66,82,122,140,158]. No meta-analyses were produced in the search.

3.2. Description of systematic reviews

Supplementary Table 3 presents the details of the included SRs. Nine SRs described MSP in predetermined body parts [35,53,55,65,66,82,122,140,158]. Two of the SRs included only prospective cohort studies [122,140], whereas the other seven SRs included both prospective and retrospective studies [35,53,55,65,66,82,158]. Only the risk factor body mass index (BMI) was extracted from the SR of Viikari-Juntura et al. [95,106,158,159], because the other factors assessed by these authors were based on a cross-sectional design. The SR of Scholten-Peeters et al. did not categorize the cohort studies' references for each factor [140]. This observation was confirmed (personal communication; G.M. Scholten-Peeters). Unfortunately these classifications were lost due to removal. Therefore the described cohort studies's references for each prognostic factor [15,23–25,30,38,46,47,58,60–62,73–75,101–105,114,115,117–119,125–131,137,139,146,148,163].

3.3. Double counting

Double counting was checked. Several cohort studies on whip-lash-associated disorders (WAD) were duplicates. Scholten-Peeters et al. [140] included 38 cohort studies on WAD in which the

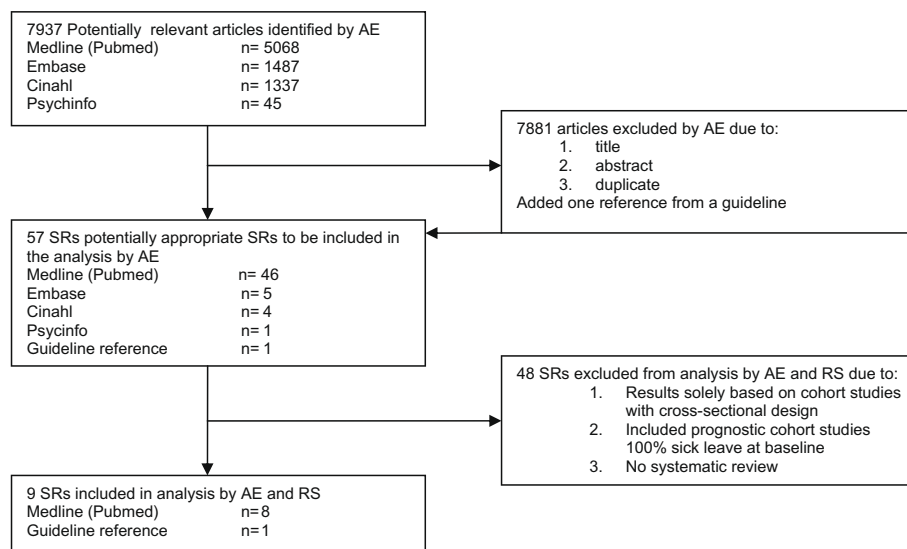


Fig. 2. Selection of systematic reviews.

subjects' accident occurred less than six days before the start of the study. Coté et al. [35] included subjects that had experienced WAD for less than six weeks [35]. Cote et al.'s SR scored less than Scholten-Peeters et al.'s SR on the methodological quality assessment. Following the preset criteria, we added one cohort study assessed by Cote et al. [82]. For LBP, the risk factor 'social support at the work place' was reviewed in two articles [55,65]. Hartvigsen et al. assessed 10 cohort studies on social support at the work place [41,42,49,63,89,92,116,143,150,170]. Hoogendoorn et al. assessed five cohort studies on the same subject [19,57,92,116,133]. Hartvigsen et al. scored 1 point more than Hoogendoorn et al. on methodological quality. Therefore, Hartvigsen's methodological quality rating of the two duplicated cohort studies was extracted [92,116]. Hamberg-van Reenen et al. included three articles reporting large lumbar flexion [17,50,53,152]. Two of these articles, both rated as having high methodological quality, were related to the same cohort study [50,152]. Thus, both were mentioned but counted as one.

3.4. Participants

The number of subjects ranged from 465 to 27,923 per SR. The included population in SRs considering risk factors consisted of working and community-based subjects. The SRs considering prognostic factors included patients from private and primary care practices, hospital emergency departments, and population- and insurance-based cohorts (Supplementary Table 3).

3.5. Risk and prognostic factors

Five SRs assessed risk factors [53,55,65,66,158]. Two of these evaluated the ICF dimension environmental factors [55,65]; two SRs addressed the dimension of body functions and structure

[53,158]; and one SR assessed factors on the activity and participation dimension [66]. Five SRs assessed prognostic factors on several dimensions of the ICF [35,55,82,122,140]. One SR included cohort studies of both the risk and prognostic factors [55].

Several SRs set the cut-off points for a positive risk estimate at >2.0 and <0.5 [35,66,82,140]. One SR used the same cut-off points to indicate the strength of the association [55]. Another SR presented prognostic factors that used these cut-off points in at least one study [82]. One SR set the criteria for a positive risk or prognostic factor at a statistically significant *p*-value of 0.10 or less [53]. Three different SRs included statistical analyses in their methodological quality assessments [65,122,158].

3.6. Outcome measurements

A large variety of questionnaires were used to assess MSP in the cohort studies, ranging from self-reported pain, disability, recovery time, sick leave, and incidence of LBP to incidence of claims (Supplementary Appendix 2). The incidence of MSP was measured to determine the risk factors. The consequences of MSP were evaluated for prognostic factors. The outcome measures in Hamberg-van Reenen et al.'s SR varied from incidence of MSP to filing of insurance claims due to MSP [53]. Overall for prognostic factors, a large variety of baseline assessments and follow-up measurements were used. New episodes were not specifically operationalized. Pincus et al.'s criterion for inclusion was acute LBP in patients who had no pain during the preceding three months [122].

3.7. Methodological quality of systematic reviews

The methodological quality of SRs is described in Table 4. Cohen's kappa for overall agreement between the reviewers was

Table 4
Methodological quality of included systematic reviews [68].

	Hartvigsen et al., 2004 [55]	Ijmker et al., 2007 [66]	Kuijpers et al., 2004 [82]	Scholten-Peeters et al., 2003 [140]	Hamberg van Reenen et al., 2007 [53]	Hoogendoorn et al., 2000 [65]	Pincus et al., 2006 [122]	Cote et al., 2001 [35]	Viikari- Juntura et al., 2007 [158]
1 Is the search strategy described in enough detail for the search to be reproducible?	+	+	+	+	+	+	+	+	+
2 Was the search for evidence reasonably comprehensive?	+	+	+	+	+	+	+	±	-
3 Were the criteria used for deciding which studies to include in the review reported?	+	+	+	+	+	+	+	+	+
4 Was bias in the selection of articles avoided?	+	+	+	+	-	-	+	+	+
5 Were the criteria used for assessing the validity of the studies that were reviewed reported?	+	+	+	+	+	+	+	+	-
6 Was the validity of all of the studies referred to in the text assessed using appropriate criteria in analysing the studies that are cited?	+	+	+	+	+	+	+	+	+
7 Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported? (Best evidence synthesis)	+	+	+	+	+	+	-	-	-
8 Were the findings of the relevant studies combined (or not combined) and analysed appropriately relative to the primary question the review addresses and the available data?	+	+	+	+	+	+	-	-	-
9 Were the conclusions made by the author(s) supported by the data and/or the analysis reported in the review?	+	+	+	+	+	+	+	±	+
Total score	9	9	9	9	8	8	7	5	5

+ = criteria 'met'; ± = criteria 'unclear' / 'partly met'; - = criteria 'not met'.

$K = 0.53$, which is considered to represent moderate agreement [4,86]. Full agreement for all criteria ($K = 1.00$) was reached during the consensus meeting. The third assessor did not come into operation. The methodological quality rating of SRs ranged from 5 to 9 points with a median of 8 points. Seven SRs had minor limitations [53,55,65,66,82,122,140]. Since they had a minimum score of 7 out of 9 points. Two had moderate limitations [35,158]. In two SRs, the selection bias could have occurred, because the selection of articles was done by one reviewer [53,65]. Three articles did not report the methods used to combine the findings, nor did these SRs combine the cohort studies appropriately [35,122,158].

3.8. Methodological quality of cohort studies

The methodological quality assessment of the cohort studies was reproduced from the included SRs. The methodological quality for each risk and prognostic factor across SRs varied widely. A criterion for clearly defining the objective of the cohort study was assessed in two SRs [55,65]. One SR described a criterion about the correct statement of the research question [35]. A clear description of the study population was a criterion in five SRs [35,55,65,82,140]. Inclusion and exclusion criteria were described in six SRs [35,53,55,82,140,122]. The response rate at baseline was an assessment criterion in six SRs and varied from a reported minimum of 80% [35,53,55,65,66,82]. A response rate less than 60% was an exclusion criterion in one SR [158]. The dropout-loss-to-follow-up rate was less than 20% in five SRs [65,66,82,140,122]. Two SRs qualitatively expressed the dropout-loss-to-follow-up as 'reasonable' but did not report a percentage [35,158]. Two other SRs rated the criteria positive for sufficient time between baseline and follow-up [53,55]. All included SRs described standardised methods for the data collection of acceptable quality of prognostic or risk factors. One SR judged the prognostic factors on clinical relevance [140]. Another SR assessed the intention of the prognostic factors, such as dose, level, and duration [35].

For the outcome measurements used in the SRs, adequate, standardised, valid, and reliable measure instruments scored one quality point in all SRs. Four SRs gained one quality assessment point, if comparison between the dropout group and the follow-up group at baseline was measured [35,53,82,122].

The data analyses described in the SRs were assessed for whether a multivariate analysis was done. A confounder control was assessed in all the SRs. Three SRs gained one quality point because the number of cases in the multivariate analyses was at least 10 times the number of independent variables [53,55,56]. Two other SRs reported sufficient numbers of subjects [82] and more than 200 subjects in the analysis sample [122].

3.9. Level of evidence based on GRADE dimensions

The level of evidence for risk and prognostic factors for MSP according to GRADE was classified within the ICF dimensions (Table 5). This level of evidence was based on the methodological quality of each SR, the methodological quality of the cohort studies included in the SRs, and the consistency of the results of the cohort studies (Table 5). Highly rated evidence is described in Section 3.9.

3.9.1. Body function and structure

3.9.1.1. Risk factors. In two SRs, 15 cohort studies reported mobility of the spine as risk or prognostic factor for MSP. The results for neck mobility were inconsistent (Table 5). One SR reported increased mobility of the lumbar spine as a risk factor for LBP [53]. The two cohort studies considered in this SR were deemed to have high methodological quality and showed the same positive direc-

tion [17,50,152]. Two articles researched the same cohort and were therefore counted as one. According to the GRADE-based assessment, high evidence was found for increased mobility of the lumbar spine is a risk factor for lumbar pain.

3.9.1.2. Prognostic factors. For two SRs [82,140], that included eight cohort studies, high evidence was found that intense pain intensity at the onset of shoulder and neck pain is a prognostic factor for the duration of symptoms [82,140]. Mental functions were investigated in a population with WAD [140]. Four included cohort studies found no association between 'high acute psychological response' after a car accident and prolonged WAD. One included cohort study found a positive association. Because more than 75% of the results pointed in the same direction, according to GRADE, it can be concluded that there is high evidence that 'high acute psychological response' is not a prognostic factor for WAD.

3.9.2. Activity and participation

3.9.2.1. Risk factors. None of the included SRs examined risk factors for MSP on the activities and participation dimension.

3.9.2.2. Prognostic factors. One SR [82] identified high-activity limitations and participation restrictions at baseline, and another SR [140] identified low workload in neck muscles and driving occupation as prognostic factors for neck and shoulder disorder [140]. The results of the included cohort studies in these SRs were all in the same positive direction for prognostic factors for neck and shoulder disorder. However, they were each based on only one high methodological quality cohort study; therefore, these SRs were rated as providing moderate evidence. High evidence could not be obtained in these SRs on the activities and participation dimension of the ICF.

3.9.3. Environmental factors

3.9.3.1. Risk factors. One high-quality SR examined low job satisfaction as a risk factor for LBP [65]. This SR included six cohort studies. Five cohort studies were rated as methodologically high quality. These five cohort studies showed positive results. One methodologically low-quality cohort study showed no results. High evidence was produced showing that low job satisfaction is a risk factor for LBP. Poor job content (defined as monotonous work, work with few possibilities for new learning and developing knowledge and skills) was rated as high evidence for not being a risk factor for low back disorder; this conclusion is based on one SR [65] that included four high-quality cohort studies showing no results. Poor social support at work (e.g., meagre social support from co-workers and supervisors, relationships at work, and problems with workmates and supervisors) was reviewed in two SRs [15,18] that assessed 13 cohort studies. According to GRADE, high evidence was produced showing that poor social support at work is not a risk factor for LBP.

3.9.3.2. Prognostic factors. There is high evidence that poor social support at work is not a prognostic factor for LBP; this conclusion is based on one SR [15] that included nine cohort studies.

3.9.4. Personal factors

3.9.4.1. Risk factors. No SR was included that measured personal factors as risk factors for MSP.

3.9.4.2. Prognostic factors. Contrary to environmental factors, personal factors are recognized but not classified in the ICF [168]. Personal factors are defined in the ICF as the background of an individual's life [168]. Fear-avoidance beliefs as a prognostic factor was measured in nine cohort studies as an individual's life

Table 5

GRADE-classified level of evidence for MSP risk and prognostic factors according to ICFdimensions.

Risk or prognostic factors					Quality of evidence							
ICF dimension		Factors identified	MSP of body part	QR	No. of cohort studies with positive or no results and methodological quality (high/low)				Summarised results	Risk factor	Prognostic factor	
					Pos		No results					
					high	low	high	low				
Body function and structure	muscle function	poor trunk muscle strength	low back	1 +[53]	5[9,10,16,50,99,100,149]		13[2,9,11,17,48,50,83,88,93,99,100,110,134,147,149,152]		no	low		
			neck	1 +[53]			1[52]		no	moderate		
		poor trunk muscle endurance	low back	1 +[53]	2[2,3,17]		1[135]		7[2,3,48,77,83,88,93,100,149,147]	no	low	
	spine mobility		neck	1 +[53]					1[9,10]	no	moderate	
		increased mobility of the lumbar spine	low back	1 +[53]	2[17,50,152]					pos	high	
		reduced mobility	low back	1 +[53]	1[17,100]		1[1]			pos	low	
			neck	1 +[53]			1[52]		1[113]	no	moderate	
	pain		neck	1 +[140]	3*	2*	1*	2*		pos		low
		pain of neck or head before collision	neck	2(1+,1±)[140,35]	2*[141]	1*	4*	1*		no		low
		high initial pain at baseline	neck	1 +[140]	4*	1*		1*		pos		high
		high pain intensity at baseline	shoulder	1 +[82]	2[96,156]					pos		high
		concomitant neck pain	shoulder	1 +[82]	1[156]					pos		moderate
		radicular symptoms	neck	1 +[140]	1*	3*	2*	5*		no		low
		sleeping disturbance	neck	1 +[140]	2*		2*			equal		low
		angular deformity	neck	1 +[140]		1*	3*	4*		no		high
		initial disc changes	neck	1 +[140]		2*	2*			no		low
		no cause of overuse	shoulder	1 +[82]	1[156]					pos		moderate
		unusual activity										
		no acute bursitis	shoulder	1 +[82]	1[156]					pos		moderate
		BMI	shoulder	1 ±[158]	3[95,106,159]					pos	moderate	
body position car accident (WAD)		unprepared for collision	neck	1 +[140]	2*		2*	2*		no		low
	turned head	neck	1 +[140]	2*		1*			pos		low	
	position velocity change > 10 km/h	neck	1 +[140]	1*		1*			equal		low	
pre-existing changes	pre-existing spondylosis + degenerative changes	neck	1 +[140]	2*	1*	2*	4*		no		low	
mental functions	cognitive impairments	neck	1 +[140]	1*			1*		pos		low	
	speed of information processing	neck	1 +[140]	1*			1*		pos		low	
	poor concentration	neck	1 +[140]	1*			1*		pos		low	
	neurotism	neck	1 +[140]	1			1		pos		low	

Activities and participation	increased acute psychological response	neck	1+[140]	1*		4*	1*	no		high
	reduced workload on neck muscle	neck	1+[140]	1*				pos		moderate
	driving occupation	neck	1+[140]	1*				pos		moderate
	high disability score at baseline	shoulder	1+[82]	1[96]	1[36]			pos		moderate
Personal factors	fear avoidance	low back	1+[122]			8[78,80,120,124,142,144,145,165]	1[29]	no		high
	depression	low back	1+[122]	1[145]				pos		moderate
	previous psychiatric problems	neck	1+[140]	1*				pos		moderate
	stress unrelated to accident	neck	1+[140]	1*			1*	pos		low
Environmental factors	nervousness	neck	1+[140]	1*				pos		moderate
	need to resume physiotherapy	neck	1+[140]		1*			pos		low
	need for cervical collar > 12 weeks	neck	1+[140]	1*			1*	pos		low
	older age	neck	1+[140]	2*	2*	10*	10*	no		high
	female gender	neck	1+[140]	3*		12*	9*	no		high
	middle age (45–54 yr)	shoulder	1+[82]	2[31,107]				pos		high
	perception of work	low back	1+[55]	1[157]	1[116]	3[43,44,63]	4[21,111,132,160,170]	no	low	
		low back	1+[55]	3[64,154,157]	3[42,153,155]	3[19,20,34,51]	10[20,45,54,57,67,85,112,116,151,167]	no		low
	low job satisfaction	low back	1+[65]	5[17,19,116,132,136]			1[57]	pos	high	
	stress at work	low back	1+[55]	1[43]		1[42]	3[49,132,170]	no	low	
		low back	1+[55]			1[42]	2[91,166]	no		moderate
	poor social support at work	low back	2+[55,65]	2[19,133]		4[42,49,57,63]	8[41,49,89,92,116,144,150,170]	no	high	
		low back	1+[55]	1[42]		4[64,153–155]	4[45,57,91,116]	no		high
	poor job content	low back	1+[65]	1[92]		4[17,92,133,136]		no	high	
	organisational aspects of work	low back	1+[55]	1[42]	1[92]	2[40,63]	5[21,49,89,143,150]	no	low	
work instruments		low back	1+[55]	2[51,57]		4[42,64,153,154]	3[142,151,166]	no		low
	low job control	low back	1+[65]			1[92]		no	moderate	
	low decision latitude	low back	1+[65]	1[57]				pos	moderate	
	high pace of work	low back	1+[65]	2[57,133]		1[18]		no	low	
	High-quality job demand	low back	1+[65]	1[57]	1[14]			pos	moderate	
	total computer use time	neck	1+[66]	1[98]		1[79]	1[69,71]	no	low	
		upper extremity	1+[66]	1[98]			1[69,71]	pos	low	
	mouse use time	neck	1+[66]	1[5,26,81,87]				pos	moderate	
		upper extremity	1+[66]	1[5,26,81,87]	1[69,71]			pos	moderate	
	keyboard use time	neck	1+[66]	1[5,26,81,87]				pos	moderate	
social contact	overload at work	upper extremity	1+[66]	1[5,26,81,87]				pos	moderate	
	social support	shoulder	1+[82]	1[106]	1[109]	1[19]		pos		moderate
		low back	1+[65]					no	low	

(continued on next page)

Table 5 (continued)

Risk or prognostic factors			QR	No. of cohort studies with positive or no results and methodological quality (high/low)	Quality of evidence				
ICF dimension	Factors identified	MSP of body part			Summarised results	Risk factor	Prognostic factor		
					Pos		No results		
					high	low	high	low	
crash position	initial treatment	neck	1 + [140]		1*		1*	pos	low
	hospital crash rear-end collision	neck	1 + [140]	1*	1*	5*	7*	no	high
	accident on highway	neck	1 + [140]	1*				pos	moderate
	car stationary	neck	1 + [140]	1*		1*	1*		low
social security services	car stationary when hit rear-end	neck	1 + [140]		1*				low
	compensation	neck	1 + [140]		1*	3*	3*	no	high

MBI = Body mass index; ICF = International Classification of Functioning, Disability and Health; MSP = musculoskeletal pain; QR = number and Quality of systematic review; + = minor limitations; ± = moderate limitations. Results of cohort studies: pos, evidence for risk or prognostic factor; no, no evidence for risk or prognostic factor; high, methodological high quality cohort study; low, methodological low quality cohort study. Summarised results: pos, evidence for a risk or prognostic factor; no, no evidence for a risk or prognostic factor; [15,23–25,30,38,46,47,58,60–62,73–75,101–105,114,115,117–119,125–131,137,139,146,148,150,163]. All the Cohort studies of Scholten-Peeters et al.

background and not as an impairment [122]. Therefore, in this SR, fear avoidance was classified on the personal factors dimension. One SR fulfilled our preset inclusion criteria [122]. Eight high-quality and one low-quality methodological cohort study concluded that fear-avoidance beliefs were not a prognostic factor for LBP. Following GRADE, we concluded that high evidence was present, showing that fear-avoidance beliefs are not a prognostic factor for LBP. High evidence was produced showing that being female and being old age are not the prognostic factors for WAD; this conclusion is based on one SR [140] that included several cohort studies. One SR [82] investigated the prognostic factor age (45–54 years) in two cohort studies rated as having high methodological quality. Following GRADE's criteria of evidence, we conclude that high evidence was produced showing that being middle aged is a prognostic factor for persistent shoulder pain.

4. Discussion

The first aim of this SR was to determine the quality of the evidence for MSP risk and prognostic factors by using findings from available SRs as a basis. There is high evidence that increased lumbar spine mobility and low job satisfaction are risk factors for the development of LBP. High evidence for prognostic factors for neck and shoulder pain are baseline neck and shoulder pain intensity, and a prognostic factor for shoulder pain is being middle aged. There is high evidence that older age, being female, angular deformity of the neck, and acute psychological response are not prognostic factors for persistent WAD. For LBP, there is high evidence that fear avoidance and poor social support at work are not prognostic factors for LBP. Poor social support at work and poor job content are not risk factors for LBP.

The second aim of this SR was to summarise the quality of evidence in terms of the ICF classification scheme to identify missing areas for further research. The ICF provides a systematic coding scheme for health information systems, establishing a common language to improve communication between different users; it also takes a neutral stand with regard to specialism and underlying theoretical models [168]. A limited number of cohort studies measured prognostic factors for MSP on the activities and participation dimension of the ICF, with all pointing towards the same positive direction for possible prognostic factors for MSP [96,36,140]. Due to the meagre number of cohort studies, none of these factors were graded as high level of evidence. In addition, no SR summarised risk factors on the ICF activities and participation dimension for the onset of MSP.

Another remarkable lack of factors could be recognized in the ICF framework. No included SRs measured the risk factors on the personal dimension. Furthermore, environmental risk and prognostic factors, such as 'work perception', were only found for LBP, not pain in other body parts. Firstly, because the present SR only included SRs, our main recommendations for future research agendas are to fill in the gaps in the ICF given in Table 5 with SRs. Secondly, if SRs are not feasible or not yet available, this table could be populated with single prospective cohort studies.

The strength of this SR lies in the number of participants included ($N = 119,849$) and in an exhaustive search of multiple electronic databases. This SR gives an overview of the systematically reviewed risk and prognostic factor literature, which consisted of longitudinal cohort studies that were all rated on methodological quality. The results of this SR with regard to prognostic factors are of clinical relevance and should have implications for practice. Psychosocial yellow flags in acute LBP are defined as risk factors for long-term disability and work loss [76]. Identification of at-risk individuals should lead to appropriate early management targeted towards the prevention of chronic pain and disability. The defini-

tion of prognostic factor is identical to these yellow flags. High neck and shoulder pain intensity could be added as yellow flags. On the other hand, with regard to LBP, fear-avoidance beliefs and poor social support at work perhaps should be removed as yellow flags [12,16,84].

As with all SRs, one limitation of the present SR is heterogeneity, which could cause effect bias. To limit the risk of bias, two reviewers independently assessed the methodological quality of the studies with a validated instrument [68], and two reviewers performed the search strategy for the second stage. Another problem inherent to all SRs is the publication bias. Because of the extent of the issue we assessed, publications could have been missed [40]. However, since we used a comprehensive search strategy, it is unlikely that any publications were missed.

The ICF defines personal factors in terms of the particular background of an individual's life and way of living and the domain mental functions as a manifestation of pathology [168]. One could argue about the ICF classification of the factors in this review. For example, the factor 'nervousness' was classified as a personal factor dimension and not as a mental impairment. Classifying these factors differently would affect the 'umbrella overview' of the existing evidence for factors, not the results of the overall quality of this SR.

Apart from the problems discussed thus far, limitations can also arise from the problems of the included SRs. For example, in assessing the risk factors for back pain, employees and community-based populations were summarised without considering the 'healthy workers effect' [97]. Indeed, workers with back pain may leave a job, resulting in a surviving workforce with healthier backs. This may introduce significant membership bias.

The outcome measurements of the primary studies were very diverse. Some measured sick leave, some measured self-reported symptoms. Self-reported physical or mental symptoms do not automatically translate to incapacity for work. One-third of the people reporting physical or mental symptoms function normally at work [162]. In the included SRs, the studies with outcome measures physical symptoms and sick leave were combined. This could have led to an effect bias. However, the variety in outcome measures and the amount of included cohort studies may have equalized possible effect bias.

In this review, cohort studies searching for prognostic factors included acute and chronic, and severe and non-severe MSP at baseline. However, we think that this heterogeneity in baseline characteristics does not significantly affect the findings of the current SR. MSP is an intermittent lifetime problem in which symptomatic periods alternate with symptom-free periods. To increase the clinical relevance, recommendations for future research should agree on outcome measures and baseline characteristics in prognostic cohort research [123].

Our recommendations for future research include performing SRs on initial pain as a prognostic factor for LBP, environmental causal factors for neck or shoulder pain, and causal personal factors for MSP. Furthermore, more methodologically high-quality cohort studies should be carried out to identify the prognostic factors categorized within the ICF activities and participation dimension. Future SRs should also assess and identify risk factors within this dimension. Effect modification of several dimensions of the ICF could occur. For example, personal factors could influence an environmental outcome variable such as job content [22,37,94]. Potential confounders and mediators such as age, gender, job satisfaction, or personal factors such as depressive feelings or motivation, should be taken into account. This SR does not provide a complete overview of the factors influencing MSP in different body parts. Thus, the next step would be to research additional SRs or to fill in the gaps given in Table 5 with cohort studies. A conceptual model of illustrating the relationship between ICF dimensions in

a working population should be built in order to gain insight into the coherence between the different dimensions in a specific population [13,164,169]. Without further research, we will not know whether modifying a person's risk factor would prevent MSP and reduce sick leave. Therefore, the risk factors 'increased mobility of the lumbar spine' and 'low job satisfaction' should not be used as selection criteria for engaging employees.

5. Conclusion

By applying the GRADE method of classifying the level of evidence, we determined that increased lumbar spine mobility and low job satisfaction are high evidence risk factors for LBP. There is high evidence that intense initial pain at baseline and being middle aged (45–54 years) are prognostic factors for neck and shoulder pain and for shoulder pain, respectively. Moreover, there is high evidence showing that older age, being female, angular deformity and acute psychological response are not prognostic factors for prolonged pain in WAD. High evidence also indicated that fear at early stages of pain and poor social support at work are not prognostic factors for LBP. In addition, high evidence indicated that poor job content and poor social support at work are not risk factors for LBP. Recommendations for future research are to systematically review prospective cohort studies on MSP risk factors on the ICF activities and participation dimension and personal dimension. Further recommendations include performing SRs on environmental risk factors for neck and shoulder pain and the prognostic factor initial pain for LBP. Finally, SRs on environmental risk and prognostic factors of MSP other than LBP are recommended.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.pain.2009.08.032](https://doi.org/10.1016/j.pain.2009.08.032).

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